

AMENDMENTS TO THE CLAIMS

Claims 2, 3, 7-10, 12, and 15-20 have been canceled. Claims 1, 4-6, 11, 13 and 14 are now pending. Claims 1, 4-6, 11, 13 and 14 have been amended as shown. This listing of claims will replace all prior versions and listings of claims in the Application.

Listing of Claims:

Claim 1 (currently amended): A method for determining that whether a human subject is at risk for developing obesity comprising ~~the steps of:~~

assaying ~~obtaining~~ a sample from a human subject, said sample comprising ~~(a)~~ a TBC1D1-encoding nucleic acid molecule or the complement thereof, ~~or (b) a TBC1D1 protein;~~ and

detecting a cytidine to thymidine alteration at the 373rd nucleotide of the TBC1D1 coding sequence of SEQ ID NO:1, an alteration in (a) said TBC1D1-encoding nucleic acid molecule or complement thereof, or (b) said TBC1D1 protein;

wherein the presence of said cytidine to thymidine alteration identifies the a subject as being at risk for developing obesity.

Claims 2 and 3 (cancelled)

Claim 4 (currently amended): The method of Claim 1 wherein said assaying ~~detection~~ step is conducted on genomic DNA ~~encoding TBC1D1~~.

Claim 5 (currently amended): The method of Claim 1 wherein said assaying ~~detection~~ step is conducted on mRNA ~~or cDNA encoding TBC1D1~~.

Claim 6 (currently amended): The method of Claim 1, wherein said cytidine to thymidine alteration ~~nucleotide variant~~ is detected by a method selected from the group consisting of:

a) hybridizing a probe specific for said alteration to RNA isolated from said human sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said alteration in the sample;

b) hybridizing a probe specific for said alteration to cDNA made from RNA isolated from said sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said alteration in the sample;

c) hybridizing a probe specific for said alteration to genomic DNA isolated from said sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said alteration in the sample;

d) amplifying all or part of said TBC1D1-encoding nucleic acid molecule, or complement thereof, in said sample using a set of primers to produce amplified nucleic acids and sequencing the amplified nucleic acids;

e) amplifying part of said TBC1D1-encoding nucleic acid molecule, or complement thereof, in said sample using a primer specific for said alteration and detecting the presence of an amplified product, wherein the presence of said product indicates the presence of said alteration in the sample;

f) molecularly cloning all or part of said TBC1D1-encoding nucleic acid molecule, or complement thereof, in said sample to produce a cloned nucleic acid and sequencing the cloned nucleic acid;

g) amplifying said TBC1D1-encoding nucleic acid molecule, or complement thereof, to produce amplified nucleic acids, hybridizing the amplified nucleic acids to a DNA probe specific said alteration and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said alteration;

h) forming single-stranded DNA from a gene fragment of said TBC1D1-encoding nucleic acid molecule, or complement thereof, from said human sample and single-stranded DNA from a corresponding fragment of a wild-type gene, electrophoresing said single-stranded DNAs on a non-denaturing polyacrylamide gel and comparing the mobility of said single-stranded DNAs on said gel to determine if said single-stranded DNA from said sample is shifted relative to wild-type and sequencing said single-stranded DNA having a shift in mobility;

i) forming a heteroduplex consisting of a first strand of nucleic acid selected from the group consisting of a genomic DNA fragment isolated from said sample, an RNA fragment isolated from said sample and a cDNA fragment made from mRNA from said sample and a second strand of a nucleic acid consisting of a corresponding human wild-type gene fragment, analyzing for the presence of a mismatch in said heteroduplex, and sequencing said first strand of nucleic acid having a mismatch;

j) forming single-stranded DNA from said TBC1D1-encoding nucleic acid molecule, or complement thereof, of said human sample and from a corresponding fragment of an allele specific for said alteration, electrophoresing said single-stranded DNAs on a non-denaturing polyacrylamide gel and comparing the mobility of said single-stranded DNAs on said gel to determine if said single-stranded DNA from said sample is shifted relative to said allele, wherein no shift in electrophoretic mobility of the single-stranded DNA relative to the allele indicates the presence of said alteration in said sample; and

k) forming a heteroduplex consisting of a first strand of nucleic acid selected from the group consisting of a genomic DNA fragment of said TBC1D1-encoding nucleic acid molecule, or complement thereof, isolated from said sample, an RNA fragment isolated from said sample and a cDNA fragment made from mRNA from said sample and a second strand of a nucleic acid consisting of a corresponding gene allele fragment specific for said alteration and analyzing for the presence of a mismatch in said heteroduplex, wherein no mismatch indicates the presence of said alteration.

Claims 7 – 10 (cancelled)

Claim 11 (currently amended): The method of claim 1, wherein said ~~assaying detection~~ step comprises hybridizing a nucleic acid probe specifically hybridizable to an altered TBC1D1 coding sequence[[,]] or complement thereof.

Claim 12 (cancelled)

Claim 13 (currently amended): A method for predicting, in a human subject, the likelihood of developing obesity associated with a genetic variant ~~variants~~ of the human *TBC1D1* gene comprising ~~detecting the presence or absence of:~~

detecting the presence of a cytidine to thymidine alteration at the 373rd nucleotide of the TBC1D1 coding sequence of SEQ ID NO:1, a nucleotide variant encoding R125W, in a TBC1D1 encoding nucleic acid of said subject; or

the amino acid substitution R125W, in a TBC1D1 protein of said subject;
wherein the presence of said cytidine to thymidine alteration ~~nucleotide variant~~, or ~~said amino acid substitution~~, predicts that said subject has an increased likelihood of developing obesity.

Claim 14 (currently amended): The method of claim 13, wherein said cytidine to thymidine alteration ~~nucleotide variant associated with obesity~~ is detected by determining the genomic sequence of said ~~TBC1D1~~ *TBC1D1* gene.

Claim 15 – 20 (cancelled)